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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,929	08/04/2003	David Wallach	WALLACH10D	4943

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

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06/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,929	WALLACH ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

NOT SURE WHICH PRIORITY DOCUMENT PC 5/29/07

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 03/06/2007, has been entered.
Claim 1 has been amended.
Claims 2-5 have been canceled.
Claim 6 has been added.

Claims 1 and 6 are pending.

2. Applicant's election of Group I, drawn to immunoassays to detect TBP-II, in the Remarks, filed 03/06/2007, is acknowledged.

Given that the only remaining claims are drawn to methods of detecting TBP-II, the previous restriction has been rendered moot.

Applicant's previous species elections of autoimmune diseases and rheumatoid arthritis in the context of the claimed methods has been acknowledged in the previous Office action, mailed 02/08/2007.

Claims 1 and 6 are under consideration as the elected invention and species.

3. Priority.

Applicant's claim for benefit of priority on page 1 of the instant specification is acknowledged.

CROSS REFERENCE TO RELATED APPLICATIONS
[0001] The present application is a division of U.S. application no. 09/800,908, filed March 8, 2001, now issued as U.S. Patent 6,602,993, which is a division of 08/477,347, filed June 7, 1995, now issued as U.S. Patent 6,232,446, which is a continuation-in-part of U.S. application no. 07/930,443, filed on August 19, 1992, and U.S. application no. 08/450,972, filed May 25, 1995, now abandoned. The entire contents of said applications are hereby incorporated herein by reference. Application no. 07/930,443, filed on August 19, 1992, is a continuation of application no. 07/524,263, filed May 16, 1990, now abandoned. Application no. 08/450,972, filed May 25, 1995, is a continuation of application no. 08/115,685, filed September 3, 1993, now abandoned.

However, the priority documents, including USSNs 07/930,443, 07/524,263 08/450,972, and 08/115,685 were not available to the examiner at this time.

Therefore, the priority for the instant claims prior to USSN 08/477,347, now issued as U.S. Patent No. 6,232,446, could not be determined at this time.

Accordingly, the instant claims appear to have an effective date of USSN 08/477,347, filed 05/25/1995.

Also, If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Also, see United States Patent and Trademark Office OG Notices: 1268 OG 89 (18 March 2003).

Therefore, given the lack of clarity of the written description of the instant claims, the claim for priority back to the USSNs filed earlier than USSN 08/477,347, filed 05/25/1995, has not been determined at this time.

In turn, given the lack of clarity of the written description of the instant claims , the claim for benefit of priority to the foreign priority documents could not be determined denied at this time because the earliest U.S. priority date could not be determined.

Therefore, it appears that the effective filing date of the instant application is the filing date of USSN 08/477,347, filed 05/25/1995.

If applicant desires priority prior to 05/25/1995; applicant is invited to point out and provide documentary support for the priority of the instant claims.
Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. 112, first paragraph.

Applicant is reminded that only foreign priority documents, filed within one (1) year of the earliest U.S. priority document having satisfied 112, first paragraph, (e.g., written description) may be relied upon for claims for benefit of priority.

4. Applicant's Information Disclosure Statements, filed 08/04/2003, 08/01/2006; 03/06/2007 are acknowledged.

Given that the paper files of the priority documents were not available to the examiner at this time, certain references of the Information Disclosure Statement were not initialed, since the examiner could not determine whether the references were available in the priority files at this time.

The examiner apologizes for any inconvenience to applicant in this matter.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ® or ™ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Appropriate corrections are required

6. Claims 1 and 6 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 1 is indefinite in that the preamble begins with a noun, but is directed towards a method. Applicant should amend the claims to clearly recite claim 1 as a method claim for clarity.

B) Claims 1 and 6 are indefinite in the recitation of "an immunoassay comprising measuring the interaction ... " and "a method of determination of over-production or under-production of TBP-II in a subject using the immunoassay of claim 1 and comparing ... " because the recitation appears incomplete by omitting essential steps or ingredients, such omission amounting to a gap between the steps. See MPEP 2172.01.

For example, there appears insufficient steps and ingredients to carry out the methods of "measuring the interaction" or determining "over-production", "under-production" and "normal levels" of TBP-II in subjects and their body fluids.

Further, the nature or metes and bounds of "the interaction" or the nature or metes and bounds of "over-production", "under-production" and "normal levels" are not defined by the claims and, the specification does not provide a standard for ascertaining the requisite degree by which one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention, encompassing a determination of TBP-II in subjects or body fluids, including defining the parameters of over-production", "under-production" and "normal levels".

C) Claim 6 is indefinite in the recitation of "TBP-II" in that they only describe the products of interest by an arbitrary protein name. While the name itself may have some notion of the activity of the protein, there is nothing in the claims, which distinctly claims the human TNF binding protein TBP-II. Applicant should particularly point out and distinctly claim the "TBP-II" by claiming sufficient characteristics associated with the protein (e.g. residues 27-214 of SEQ ID NO: 3; see Claim 1). Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what that protein is and what the compositions are made up of.

D) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

7. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1 and 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with clinical diagnosis in patients. Since the detection of a disorder/disease can be disorder/disease-dependent, it is not clear that reliance on the in vitro and in vivo observations as well as the clinical experience with targeting various inflammatory conditions with anti-human TBP-II (p75 TNF receptor) accurately reflects the relative ability or efficacy of the claimed "immunoassays" or "methods of determination" to determine over-production or under-production of TBP-II in body fluids or subjects.

Several variables are used in evaluating the predictability of detection or diagnostic assays. These include diagnostic specificity and sensitivity and positive and negative predictive values.

The diagnostic sensitivity of an assay reflects the fraction of those subjects with a specific disease that the assay correctly identifies as positive.

The diagnostic specificity of an assay reflects the fraction of those subjects without the disease that the assay correctly identifies as negative.

The positive predictive value refers to the probability that an individual with a positive test result has the disease.

The negative predictive value refers to the probability that an individual with a negative test result does not have the disease.

There is an inverse relationship between the sensitivity and specificity, which is related to the assigned cutoff value that is used for a particular test to segregate diseased populations from those with no disease.

While the instant specification discloses that TBP-II-specific antibodies can serve as diagnostic tools based upon immunoassays to detect under-production or over-production of TBP-II by cells in the body in certain disorders such as cancer or autoimmune disease (e.g., see paragraph [0054] in the instant specification).

The disclosure of Example 4 in the instant specification of determining the levels of TBP-II in humans is acknowledged. While normal levels of TBP-II in human serum of healthy individuals as determined by ELISA is disclosed, it is not clear whether values of under-production and over-production were determined in the described patients with cancer, SLE or pregnancy.

Also, normal values of different body fluids do not appear to be described.

The p75 tumor necrosis factor receptor (i.e.. TBP-II) is present on nearly all cell types studies except for erythrocytes and unstimulated lymphocytes. Further, soluble TNF-binding proteins such as TBP-II have been found in urine and serum, but have a short half-life (e.g. 30 minutes to two (2) hours)

While the activity of TNF is regulated at the level of secretion and receptor expression as well as to the action of the mediators (e.g., cytokines, soluble receptors), there is insufficient guidance and direction as to the determination and, in turn, the correlation of determining the under-production or over-production of TBP-II in various body fluids as well as subjects as broadly encompassed by the claimed invention.

For example, there appears to be insufficient guidance as to the critical steps, ingredients and endpoints (e.g., normal, under-production, over-production values) to carry out the methods of "measuring the interaction" or determining "over-production", "under-production" and "normal levels" of TBP-II in subjects and their body fluids.

Further, there appears to be insufficient guidance as to the nature or scope of "the interaction" or the nature or scope of "over-production", "under-production" and "normal levels", which do not appear to be defined by the claims and, the specification does not provide a standard for ascertaining the requisite degree by which one of ordinary skill in the art would not be reasonably apprised of how to make and use TBP-II-specific antibodies to determine of TBP-II in subjects or body fluids, including defining the parameters of over-production", "under-production" and "normal levels" as well as the diagnosis of various diseases or conditions, including cancer or autoimmunity (e.g., see paragraph [0054] of the specification).

In the absence of objective evidence to the contrary and keeping with the nature of evaluating a number of potential immunological markers for detection or diagnosis, the skilled artisan would predict that there is an overlap between diseased and non-diseased groups, since there is insufficient guidance and direction as how to predict what levels are relied upon for detecting under-production or over-production of TBP-II in normal or diseased individuals. For example, individuals with the disease may exhibit normal levels of TBP-II in their body fluids.

Here, applicant has not provided sufficient direction and guidance as to the sensitivity and specificity of detecting a normal, under-production or over-production of TBP-II in normal or individuals with disorders such as cancer or autoimmunity involving measuring the interaction (e.g., binding) of TBP-II with TBP-II-specific antibodies alone.

Here, applicant has not set forth sufficient normal values as well as those values that would lead the skilled artisan to predict the ability to detect normal, under-production or over-production of TBP-II in individuals, including the ability to detect or diagnose a disorder involving TBP-II via the use of TBP-II-specific antibodies alone.
For example, the cutoff value for a particular assay will determine the diagnostic sensitivity and specificity of the test based on the number of individuals that are diagnosed with and without the disease.

There is insufficient objective evidence that the claimed assay which relies upon the detection of TBP-II in any body fluid obtained from various individuals or patients provides the requisite sensitivity and specificity to be useful for the claimed purpose detecting normal, under-production or over-production of TBP-II in individuals, including the ability to detect or diagnose a disorder involving TBP-II via the use of TBP-II-specific antibodies alone.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

It does not appear that there is sufficient information to set forth the particular TBP-II levels, which correlates to a normal value in any body fluid, and, in turn, the values that would read on under-production or over-production of TBP-II in a broad range of individuals or diseases (e.g., cancer, autoimmunity). The specification does not teach how to extrapolate data obtained from the expression of TBP-II in human serum of certain individuals (e.g., see Example 4 on page 30 of the specification) to detecting normal, under-production or over-production of TBP-II in individuals, including the ability to detect or diagnose a disorder involving TBP-II via the use of TBP-II-specific antibodies alone, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the correlations of determining TBP-II in individuals to detect under-production or over-production of TBP-II, as well as to use such information to detect or to diagnose a disorder or a disease, broadly encompassed by the claimed methods. There is insufficient guidance and direction as well as objective evidence to provide for detecting normal, under-production or over-production of TBP-II in individuals, including the ability to detect or diagnose a disorder involving TBP-II via the use of TBP-II-specific antibodies alone or to diagnose the diversity and scope of disorders / diseases encompassed by the claimed methods.

In view of the lack of predictability of the art to which the invention pertains the lack of established protocols for effective methods to detect or diagnose the scope of inflammatory conditions, disorders and/or diseases with TBP-II-specific antibody-based assays, undue experimentation would be required to practice the claimed methods of determining normal, under-production or over-production of TBP-II in individuals, including the ability to detect or diagnose a disorder involving TBP-II via the use of TBP-II-specific antibodies alone with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for detecting normal, under-production or over-production of TBP-II in individuals, including the ability to detect or diagnose a disorder involving TBP-II via the use of TBP-II-specific antibodies alone, broadly encompassed by the claimed methods.

9. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

The specification broadly describes and the claims recite as part of the invention "TBP-II".

The specification does not provide sufficient written description for any TBP-II molecule as the target of TBP-II-specific antibodies, broadly encompassed by the claimed invention.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

Applicant has not disclosed the common structure essential for the function of TBP-II to serve as the p75 tumor necrosis factor receptor and the claims do not require any particular structure basis or testable functions be shared by the instant "TBP-II".

Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required.

It does not appear based upon the limited disclosure of antibodies that bind the TBP-II set forth in the residues 27-214 of SEQ ID NO: 3 alone that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the limited number of species disclosed and the extensive variation permitted within the genus of "TBP-II".

"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d, 1398, (Fed. Cir. 1997).

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406.

In the absence of disclosure of relevant, identifying characteristics of the "TBP-II", there is insufficient written disclosure under 35 U.S.C. 112, first paragraph.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 1115).

Applicant is invited to consider amending the claimed "TBP-II" to recite the residues 27-214 of SEQ ID NO: 3 as recited in instant Claim 1 and disclosed in the specification as filed to obviate this rejection.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Given the issues of priority addressed above in that the examiner could not establish the earliest U.S. priority date for the instant claims at this time, the following rejections are applied under 35 U.S.C. 102(a)(b)(e) until such time the earliest U.S. priority date for the instant claims can be established.

The examiner apologizes for any inconvenience to applicant in this matter.

However, again, applicant is invited to establish the earliest U.S. priority date for the instant claims with documentary support.

13. Claims 1 and 6 are rejected under 35 U.S.C. § 102(a)(b) as being anticipated by Brockhaus et al. (EP 0334165, published 09/2719/89) (see entire document).

Brockhaus et al. teaches antibodies to TNF receptor (see columns 3-6, Examples and Claims) and their use as diagnostic tools for the determination of TNF receptors on the cell surface and of soluble forms, including tissues samples with assays well known in the art (see columns 5-6, overlapping paragraph and Claim 21).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations of measuring the interaction of TBP-II with TBP-II-specific antibodies and determining said levels in comparison to normal values would be inherent properties of the referenced methods to detect TNF receptors in cells and tissues in diagnostic assays.

Although the reference does not explicitly indicated that one compares levels with normal values, such assays required comparison to normal values for proper analysis. Therefore, the ordinary artisan would have immediately envisaged carrying out immunoassays with controls and in the case with diagnostic assays, normal and healthy human values were employed as the proper controls and comparison for determining values that are either above or below the values observed in normal healthy individuals at the time the invention was made.

There does not appear to be any manipulative differences between the prior art disclosure and the instant methods.

Although the prior art does not disclose the terminology TBP-II or SEQ ID NO: 3 per se, it appears that the prior art and the instant claims are drawn to the same p75 tumor necrosis factor receptors.

Comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons. The burden is on the applicant to establish a patentable distinction between the claimed and referenced tumor necrosis factor binding proteins or receptors.

14. Claims 1 and 6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brockhaus et al. (EP 0334165, published 09/2719/89) in view of Wolpe et al. (U.S. Patent No. 5,700,466) (see entire document).

Brockhaus et al. (EP 0334165) teach antibodies to TNF receptor (see column 3, paragraph 5; column 9, paragraphs 4-5, Example 3) and their use as diagnostic tools for the determination of TNF receptors on the cell surface and of soluble forms, including tissues samples with assays well known in the art (see columns 5-6, overlapping paragraph and Claim 21) (see entire document).

Although the prior art does not disclose the terminology TBP-II or SEQ ID NO: 3 per se, it appears that the prior art and the instant claims are drawn to the same p75 tumor necrosis factor receptors.

Comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons. The burden is on the applicant to establish a patentable distinction between the claimed and referenced tumor necrosis factor binding proteins or receptors.

Brockhaus et al. (EP 0334165) differs from the claimed invention by not disclosing comparing the over-production and under production of TBP-II in immunoassays to detect tumor necrosis factor binding proteins.

In addition, Wolpe et al. (U.S. Patent No. 5,700,466) (see entire document) has been added to provide further evidence that diagnostic assays, including those associated with TNF and related diseases, were well known and practiced at the time the invention was made. For example, Wolpe et al. indicates that the use of antibodies for diagnosis purposes has been extensively described in the literature (e.g., see column 7, lines 20-22).

Although the references do not explicitly indicated that one compares levels with normal values, such assays required comparison to normal values for proper analysis. Therefore, the ordinary artisan would have immediately envisaged carrying out immunoassays with controls and in the case with diagnostic assays, normal and healthy human values were employed as the proper controls and comparison for determining values that are either above or below the values observed in normal healthy individuals at the time the invention was made.

Given the role of TNF and/or cellular /soluble TNF receptors in various disease conditions as taught by the prior art, one of ordinary skill in the art at the time the invention was made would have been motivated to select TNF-receptor-specific antibodies for various immunoassays well known in the art to detect and determine the levels TNF receptors in various tissues and body fluids to determine their presence in various disease conditions as well as to monitor the effectiveness of treatment of said diseases, as taught by Wolpe et al. (e.g., see column 6, paragraph 3 – column 7) and Brockhaus et al. (see columns 5-6, overlapping paragraph and Claim 21). The ordinary artisan would have had an expectation of success in determining levels of TNF receptors in the various tissues and body fluids, given the prior art teachings of detecting TNF and TNF receptors and the presence of said molecules in certain disease conditions.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 550 U.S. , 2007 U.S. LEXIS 4745, 2007 WL 1237837, at *12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to determine the expression of TNF receptors in disease conditions as well as during the treatment of said disease conditions, determining the under-expression or the over-expression of TNF receptors and comparing such values to normal healthy individuals was routine to the ordinary artisan at the time the invention was made and therefore obvious in designing such immunoassays for detecting TNF receptors.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

15. Claims 1 and 6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brockhaus et al. (EP 0334165, published 09/2719/89) in view of Wolpe et al. (U.S. Patent No. 5,700,466)
as applied to claims 1 and 6 above and further in view of
Brockhaus et al. (U.S. Patent No. 5,610,279) (see entire document).

Brockhaus et al. (EP 0334165, published 09/2719/89) in view of Wolpe et al. (U.S. Patent No. 5,700,466) has been taught above.

Brockhaus et al. (U.S. Patent No. 5,610,279) has been added to provide more evidence for the structure of the TNF binding proteins of the prior art, including a clearer indication of the p75 tumor necrosis factor receptor that reads on the instant TBP-II, than a reading of Brockhaus et al. (EP 0334165) may indicate.

Brockhaus et al. (U.S. Patent No. 5,610,279) teaches the structure of the p75 tumor necrosis factor that reads on the instant TBP-II, including providing a nucleotide sequence and a deduced amino acid sequence for the cDNA (e.g., see Detailed Description, Examples and Figure 4).

Further, Brockhaus et al. (U.S. Patent No. 5,610,279) teaches antibodies to TNF receptor (see columns 3-6, Examples and Claims) and their use as diagnostic tools for the determination of TNF receptors on the cell surface and of soluble forms, including tissues samples with assays well known in the art (see columns 5-6, overlapping paragraph and Claim 21) (see entire document).

For the reasons above, the ordinary artisan had both the motivation and expectation of success in determining levels of TNF receptors in the various tissues and body fluids, given the prior art teachings of detecting TNF and TNF receptors and the presence of said molecules in certain disease conditions. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

16. No claim allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

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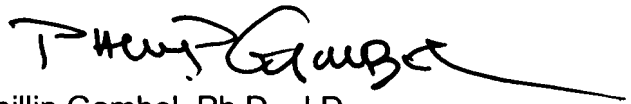

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